

DOCUMENT-IDENTIFIER: VS 5874479 A

TITLE: Therapeutic permeation enhanced wound healing compositions and methods for preparing and using same

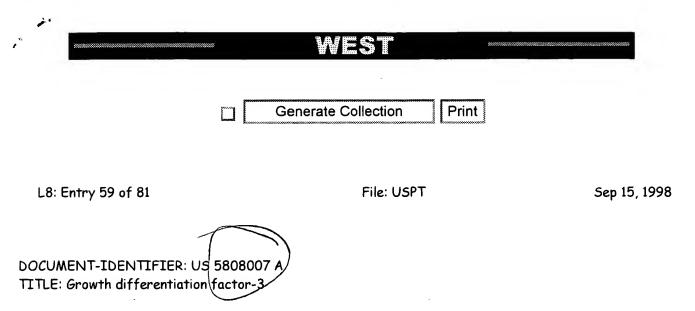
## Detailed Description Paragraph Right (220):

Nonlimiting illustrative examples of immunostimulating agents may be selected from the group consisting of betafectin.RTM, and Freund's complete adjuvant. Nonlimiting illustrative examples of cytotoxic agents may be selected from the group consisting of epithelial cell cohesiveness reducers, dermatological abradants, anti-inflammatories, lipid regulating agents, centrally acting anticholinesterases, chemotherapeutic drugs, and gastric irritants. Nonlimiting illustrative examples of antiviral agents may be selected from the group consisting of acyclovir, foscarnet sodium, ribavirin, vidarabine, ganeiclovir sodium, zidovudine, phenol, amantadine hydrochloride, and interferon alfa-n3. Nonlimiting illustrative examples of antikeratolytic agents may be selected from the group consisting of salicylic acid, lactic acid, and urea. Nonlimiting illustrative examples of anti-inflammatory agents may be selected from the group consisting of ibuprofen, naproxen, sulindac, diflunisal, piroxicam, indomethacin, etodolac, meclofenamate sodium, fenoproben calcium, ketoprofen, mefenamic acid, nabumetone, ketorolac tromethamine, diclofenac, evening primrose oil, acetylsalicylic acid, mesalamine, salsalate, diflunisal, salicylsalicylic acid, choline magnesium trisalicylate, flunisolide, triamcinoline, triamcinoline acetonide, beclomethasone diproprionate, betamethasone diproprionate, hydrocortisone, cortisone, dexamethasone, prednisone, methyl prednisolone, and prednisolone. Nonlimiting illustrative examples of antifungal agents may be selected from the group consisting of lactic acid, sorbic acid, miconazole, clotrimazole, tioconazole, terconazole, povidone-iodine, and butoconazole. Nonlimiting illustrative examples of sunscreen agents may be selected from the group consisting of ethylhexyl p-methoxycinnamate, octyl methoxycinnamate, octyl dimethyl p-aminobenzoic acid, 2-ethylhexyl salicylate, octyl salicylate, menthyl anthranilate, octocrylene, padimate o, titanium dioxide, urea, and oxybenzone. Nonlimiting illustrative examples of topical antihistamine agents may be selected from the group consisting of diphenhydramine hydrochloride and pramoxine hydrochloride. Nonlimiting illustrative examples of antibacterial agents may be selected from the group consisting of bismuth compounds, such as bismuth aluminate, bismuth subcitrate, bismuth subgalate, bismuth subsalicylate; the sulfonamides; the nitrofurans, such as nitrofuirazone and nitrofurantoin; furazolidone, metronidazole, tinidazole, nimorazole, benzoic acid, the aminoglycosides; such as gentamicin, neomycin, kanamycin, and streptomycin; the macrolides, such as erythromycin, clindamycin, and rifamycin; the penicillins, such as penicillin G, penicillin V, Ampicillin and amoxicillin; the polypeptides, such as bacitracin and polymyxin; the tetracyclines, such as tetracycline, chlorotetracycline, oxytetracycline, and doxycycline; the cephalosporins, such as cephalexin and cephalothin; and chloramphenicol, and clidamycin. Nonlimiting illustrative examples of transforming growth factors may be selected from the group consisting of Type I TGF-beta, Type 2 TGF-beta, Type 3 TGF-beta, Type 4 TGF-beta, and Type 5 TGF-beta.

CLAIMS:

31. The augmented permeation enhanced-wound healing composition according to claim 19, wherein the medicament useful for treating wounds is a transforming growth factor selected from the group consisting of Type 1 <u>TGF</u>-beta, Type 2 <u>TGF</u>-beta, Type 3 <u>TGF-beta, Type 4 TGF-beta, and Type 5 <u>TGF</u>-beta.</u>

(15 Pat 5874,479



## Detailed Description Paragraph Table (3):

 $(xi) \ SEQUENCE \ DESCRIPTION: \ SEQ \ ID \ NO:17: \ LysArgHisAlaArgArgProThrArgArgLysAsnHisAspAspThr$ 

151015 CysArgArgHisSerLeuTyrValAspPheSerAspValGlyTrpAsp 202530

AspTrpIleValAlaProLeuGlyTyrAspAlaTyrTyrCysHisGly 354045

LysCysProPheProLeuAlaAspHisPheAsnSerThrAsnHisAla 505560

ValValGInThrLeuValAsnAsnMetAsnProGlyLysValProLys 65707580

AlaCysCysValProThrGlnLeuAspSerValAlaMetLeuTyrLeu 859095

AsnAspGlnSerThrValValLeuLysAsnTyrGlnGluMetThrVal 100105110 ValGlyCysGlyCysArg 115 (2)

INFORMATION FOR SEQ ID NO:18: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 119 amino acids (B)

TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (vii)

IMMEDIATE SOURCE: (B) CLONE: BMP-3 (ix) FEATURE: (A) NAME/KEY: Protein (B) LOCATION: 1..119 (xi)

SEQUENCE DESCRIPTION: SEQ ID NO:18: GInThrLeuLysLysAlaArgArgLysGInTrpIleGluProArgAsn 151015

CysAlaArgArgTyrLeuLysValAspPheAlaAspIleGlyTrpSer 202530

GluTrpIleIleSerProLysSerPheAspAlaTyrTyrCysSerGly 354045

AlaCysGlnPheProMetProLysSerLeuLysProSerAsnHisAla 505560

ThrIleGInSerIleValArgAlaValGlyValValProGlyIlePro 65707580

GluProCysCysValProGluLysMetSerSerLeuSerIleLeuPhe 859095

PheAspGluAsnLysAsnValValLeuLysValTyrProAsnMetThr 100105110 ValGluSerCysAlaCysArg 115 (2)

INFORMATION FOR SEQ ID NO:19: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 115 amino acids (B)

TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (vii)

IMMEDIATE SOURCE: (B) CLONE: MIS (ix) FEATURE: (A) NAME/KEY: Protein (B) LOCATION: 1..115 (xi)

SEQUENCE DESCRIPTION: SEQ ID NO:19: ProGlyArgAlaGlnArgSerAlaGlyAlaThrAlaAlaAspGlyPro 151015

CysAlaLeuArgGluLeuSerValAspLeuArgAlaGluArgSerVal 202530

LeuIleProGluThrTyrGlnAlaAsnAsnCysGlnGlyValCysGly 354045

TrpProGlnSerAspArgAsnProArgTyrGlyAsnHisValValLeu 505560

LeuLeuLysMetGlnAlaArgGlyAlaAlaLeuAlaArgProProCys 65707580

CysValProThrAlaTyrAlaGlyLysLeuLeuIleSerLeuSerGlu 859095

GluArgIleSerAlaHisHisValProAsnMetValAlaThrGluCys 100105110 GlyCysArg 115 (2) INFORMATION FOR

SEQ ID NO:20: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 121 amino acids (B) TYPE: amino acid (C)

STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (vii) IMMEDIATE SOURCE: (B)

CLONE: Inhibin alpha (ix) FEATURE: (A) NAME/KEY: Protein (B) LOCATION: 1..121 (xi) SEQUENCE

DESCRIPTION: SEQ ID NO:20: LeuArgLeuLeuGlnArgProProGluGluProAlaAlaHisAlaAsn 151015

CysHisArgValAlaLeuAsnIleSerPheGlnGluLeuGlyTrpGlu 202530

ArgTrpIleValTyrProProSerPheIlePheHisTyrCysHisGly 354045

```
http://westbrs:8002/bin/gate.exe?f=doc&sta...age=&p_Message=&p_doccnt=1&p_doc_1=PTFKWIC
'ĠlyCysGlyLeuHisIleProProAsnLeuSerLeuProValProGly 505560
AlaProProThrProAlaGInProTyrSerLeuLeuProGlyAlaGIn 65707580
ProCysCysAlaAlaLeuProGlyThrMetArgProLeuHisValArg 859095
ThrThrSerAspGlyGlyTyrSerPheLysTyrGluThrValProAsn 100105110 LeuLeuThrGlnHisCysAlaCysIle 115120 (2)
INFORMATION FOR SEQ ID NO:21: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 121 amino acids (B)
TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (vii)
IMMEDIATE SOURCE: (B) CLONE: Inhibin beta A (ix) FEATURE: (A) NAME/KEY: Protein (B) LOCATION:
1..121 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:
ArgArgArgArgArgGlyLeuGluCysAspGlyLysValAsnIleCys 151015
CysLysLysGlnPhePheValSerPheLysAspIleGlyTrpAsnAsp 202530
TrpIleIleAlaProSerGlyTyrHisAlaAsnTyrCysGluGlyGlu 354045
CysProSerHisIleAlaGlyThrSerGlySerSerLeuSerPheHis 505560
SerThrValIleAsnHisTyrArgMetArgGlyHisSerProPheAla 65707580
AsnLeuLysSerCysCysValProThrLysLeuArgProMetSerMet 859095
LeuTyrTyrAspAspGlyGlnAsnIleIleLysLysAspIleGlnAsn 100105110 MetIleValGluGluCysGlyCysSer 115120 (2)
INFORMATION FOR SEQ ID NO:22: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 120 amino acids (B)
TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (vii)
IMMEDIATE SOURCE: (B) CLONE: Inhibin beta B (ix) FEATURE: (A) NAME/KEY: Protein (B) LOCATION:
1..120 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:
ArgIleArgLysArgGlyLeuGluCysAspGlyArgThrAsnLeuCys 151015
CysArgGlnGlnPhePheIleAspPheArgLeuIleGlyTrpAsnAsp 202530
TrpIleIleAlaProThrGlyTyrTyrGlyAsnTyrCysGluGlySer 354045
CysProAlaTyrLeuAlaGlyValProGlySerAlaSerSerPheHis 505560
ThrAlaValValAsnGlnTyrArgMetArgGlyLeuAsnProGlyThr 65707580
ValAsnSerCysCysIleProThrLysLeuSerThrMetSerMetLeu 859095
TyrPheAspAspGluTyrAsnIleValLysArgAspValProAsnMet 100105110 IleValGluGluGluCysGlyCysAla 115120 (2)
INFORMATION FOR SEQ ID NO:23: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 114 amino acids (B)
TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (vii)
IMMEDIATE SOURCE: (B) CLONE: TGF-beta 1 (ix) FEATURE: (A) NAME/KEY: Protein (B) LOCATION: 1..114
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23: ArgArgAlaLeuAspThrAsnTyrCysPheSerSerThrGluLysAsn
151015 CysCysValArgGlnLeuTyrIleAspPheArgLysAspLeuGlyTrp 202530
LysTrpIleHisGluProLysGlyTyrHisAlaAsnPheCysLeuGly 354045
ProCysProTyrIleTrpSerLeuAspThrGlnTyrSerLysValLeu 505560
AlaLeuTyrAsnGlnHisAsnProGlyAlaSerAlaAlaProCysCys 65707580
ValProGlnAlaLeuGluProLeuProIleValTyrTyrValGlyArg 859095
LysProLysValGluGlnLeuSerAsnMetIleValArgSerCysLys 100105110 CysSer (2) INFORMATION FOR SEQ ID
NO:24: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 114 amino acids (B) TYPE: amino acid (C)
STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (vii) IMMEDIATE SOURCE: (B)
```

CLONE: TGF-beta 2 (ix) FEATURE: (A) NAME/KEY: Protein (B) LOCATION: 1...114 (xi) SEQUENCE

DESCRIPTION: SEQ ID NO:24: LysArgAlaLeuAspAlaAlaTyrCysPheArgAsnValGlnAspAsn 151015

CysCysLeuArgProLeuTyrIleAspPheLysArgAspLeuGlyTrp 202530

LysTrpIleHisGluProLysGlyTyrAsnAlaAsnPheCysAlaGly 354045

AlaCysProTyrLeuTrpSerSerAspThrGlnHisSerArgValLeu 505560

SerLeuTyrAsnThrIleAsnProGluAlaSerAlaSerProCysCys 65707580

ValSerGlnAspLeuGluProLeuThrIleLeuTyrTyrIleGlyLys 859095

ThrProLysIleGluGlnLeuSerAsnMetIleValLysSerCysLys 100105110 CysSer (2) INFORMATION FOR SEQ ID

NO:25: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 114 amino acids (B) TYPE: amino acid (C)

STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (vii) IMMEDIATE SOURCE: (B)

CLONE: <u>TGF</u>-beta 3 (ix) FEATURE: (A) NAME/KEY: Protein (B) LOCATION: 1..114 (xi) SEQUENCE

DESCRIPTION: SEQ ID NO:25: LysArgAlaLeuAspThrAsnTyrCysPheArgAsnLeuGluGluAsn 151015

ĆysCysValArgProLeuTyrIleAspPheArgGInAspLeuGlyTrp 202530

LysTrpValHisGluProLysGlyTyrTyrAlaAsnPheCysSerGly 354045

ProCysProTyrLeuArgSerAlaAspThrThrHisSerThrValLeu 505560

GlyLeuTyrAsnThrLeuAsnProGluAlaSerAlaSerProCysCys 65707580

ValProGlnAspLeuGluProLeuThrIleLeuTyrTyrValGlyArg 859095

ThrProLysValGluGlnLeuSerAsnMetValValLysSerCysLys 100105110 CysSer (2) INFORMATION FOR SEQ ID

NO:26: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 116 amino acids (B) TYPE: amino acid (C)

STRANDEDNESS: single (D) TOPOLOGY: linear (ii) MOLECULE TYPE: protein (vii) IMMEDIATE SOURCE: (B)

CLONE: TGF-beta 4

Chypoter 1

Chypoter 2

Chypoter 3

Chy

3 of 3